D_2/D_3 Competition. The product mole ratio c/b is given by eq 20, obtained by dividing eq 18 by eq 19 and substituting the definition of P_2 (see above). From the slope (m_3) and intercept (b_3) of this equation one obtains values for P_3 and S_4 (eq 21 and 22). With the value of m_{2b} from the case above one can obtain a third independent estimate of P_2 (eq 23).

$$c = k_H^{DD}d_2 + 3k_D^{DD}d_3 \quad (18)$$

$$b = 2k_D^{HD}d_2 + 2k_H^{HD}d_1 \quad (19)$$

$$(1 + P_2d_1/d_2)(c/b) = (3k_D^{DD}/2k_D^{HD})(d_3/d_2) + k_H^{DD}/2k_D^{HD} \quad (20)$$

$$P_3 = 3b_3/m_3 \quad (21)$$

$$S_4 = 3/2m_3 \quad (22)$$

$$P_2 = b_3m_{2b} \quad (23)$$

D_0/D_3 Competition. If there are small amounts of D_2 impurity in D_3, product formation under pseudo-first-order conditions will be given by eq 24 and 25, and the product mole ratio c/a will be given by eq 26. The latter is solved by substituting for $k_H^{DD}/3k_H^{HH}$ the value $1/3S_1S_2$ (or simply $1/3S^2$) as determined by the foregoing analysis (via. Table II).

$$a = 3k_H^{HH}d_0 \quad (24)$$

$$c = 3k_D^{DD}d_3 + k_H^{DD}d_2 \quad (25)$$

$$c/a = (3k_D^{DD}/3k_H^{HH})(d_3/d_0) + (k_H^{DD}/3k_H^{HH})(d_2/d_0) = [k_D^{DD}/k_H^{HH} + (k_H^{DD}/3k_H^{HH})(d_2/d_3)](d_3/d_0) \quad (26)$$

Acknowledgment. Financial support for this investigation was provided through National Institutes of Health Grants GM-31910 and RR-5606.

Amelioration of the Conjugate Addition Chemistry of α-Alkoxycopper Reagents: Application to the Stereospecific Synthesis of *C*-Glycosides

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Abstract: ((Benzyloxy)methyl)- and [((tetrahydropyran-2-yl)oxy)methyl]lithium reagents were synthesized via transmetalation of the corresponding α-alkoxystannanes. These lithium reagents were converted into a number of organocopper reagents, and their reactivity with three enones of differing steric demand was examined. The effect of copper(I) precursor as well as additives such as boron trifluoride etherate and chlorotrimethylsilane was examined in detail. Application of this technology to a pair of isomeric tri-*n*-butylstannyl glucopyranosides reveals the scope and limitations for the stereospecific synthesis of *C*-glycosides via conjugate addition reactions to enones.

Despite problems involved in their generation and handling, α-heteroatom substituted lithium reagents have seen extensive application in organic synthesis.[2] Surprisingly, the use of these valuable reagents in copper(I)-mediated conjugate addition reactions has been rare.[3-8] In surveying literature citations related to the general phenomenon of reaction success as a function of copper(I) source purity,[9] we became suspicious that the limited number of applications of (α-alkoxymethyl)cuprates might have been a direct consequence of reagent sensitivity to impurities in the copper(I) source.

As a result of these considerations, it was decided to examine the conjugate addition reactions of several (α-alkoxymethyl)copper reagents. The goal of such experiments was threefold: (1) to determine the sensitivity of these reagents both to handling and copper(I) source purity, (2) to determine the reactivity of these reagents with enones of increasing steric demand, and (3) to minimize the number of equivalents of (α-alkoxymethyl)lithium

(1) Proctor and Gamble Fellow 1985-1986.

(2) The chemistry of α-alkoxylithium reagents is becoming a relatively mature field, and the preparation of these reagents is possible via transmetalation of α-alkoxystannanes,[2a-g] reductive cleavage of α-alkoxy sulfides,[2h,i] and direct metalation of ethers.[2j,3] (a) Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927. (b) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (c) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201. (d) Burke, S. D.; Shearouse, S. A.; Burch, D. J.; Sutton, R. W. *Tetrahedron Lett.* **1980**, *21*, 1285. (e) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1982**, *47*, 5422. (f) McGarvey G. J.; Kimura, M. *J. Org. Chem.* **1985**, *50*, 4655. (g) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3163. (h) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6902. (i) Cohen, T.; Lin, M.-T. *J. Am. Chem. Soc.* **1984**, *106*, 1130. (j) Lehmann, R.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 745.

(3) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3165.

(4) Eckrich, T. M. Ph.D. Thesis, Harvard University, 1984.

(5) An indirect procedure to produce γ-hydroxy ketones via conjugate addition to enones involves the 1,4 addition of vinylcuprate followed by ozonolysis and selective reduction of the γ-ketoaldehyde: Jones, T. K.; Denmark, S. E. *J. Org. Chem.* **1985**, *50*, 4037. These authors report the specific failure to utilize ((benzyloxy)methyl)cuprate due to formation of the dimerized product, 1,2-bis(benzyloxy)ethane.

(6) Another indirect procedure to achieve the conjugate addition of the α-alkoxymethyl moiety involves reaction of enones with (α-silylmethyl)-cuprates, followed by oxidative insertion to yield the α-siloxymethyl derivative: Tamao, K; Ishida, N. *Tetrahedron Lett* **1984**, *25*, 4249.

(7) There have also been several reports of (*di*alkoxymethyl)cuprate 1,4-addition to enones: (a) Quintard, J.-P.; Elissondo, B.; Pereyre, M. *J. Organomet. Chem.* **1981**, *212*, C31. (b) Shiner, C. S.; Tsunoda, T.; Goodman, B. A.; Lee, S.-H. *Abstracts of Papers*, 192nd National Meeting of the American Chemical Society, Anaheim, CA; American Chemical Society: Washington, DC, 1986; Abstract 227.

(8) After this work was submitted for publication in its original form, a communication appeared concerning α-alkoxycopper reagents: Linderman, R. J.; Godfrey, A. *Tetrahedron Lett.* **1986**, *27*, 4553.

(9) A number of reports have appeared concerning experimental difficulties or outright failure of cuprate reactions as a consequence of poor quality of the copper(I) source: (a) Smith, J. G.; Wikman, R. T. *Synth. React. Inorg. Met.-Org. Chem.* **1974**, *48* 239. (b) House, H. O.; Wilkins, J. M. *J. Org. Chem.* **1978**, *43*, 2443. (c) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. (d) Iyer, R. S.; Helquist, P. *Org. Synth.* **1985**, *64*, 1. (e) Lipschutz, B. H.; Whitney, S.; Kozlowski, J. A.; Breneman, C. M. *Tetrahedron Lett.* **1986**, *27*, 4273.

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Scheme I

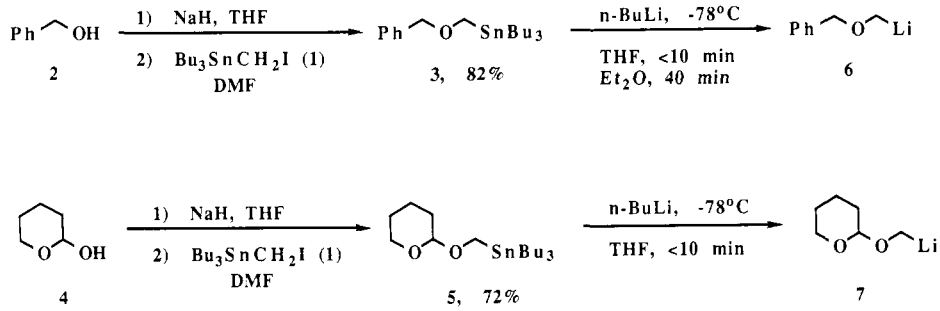


Table I. Reactions of Organocopper Reagents **8–12** with Enones **13–15**

run	reagent	conditions	total equiv of $ROCH_2Li$ employed	yields of conjugate addition products, %		
				16a,b	**17a,b**	**18a,b**
A_{1-3}	$(PhCH_2OCH_2)_2CuLi$ (**8a**)	THF–DIPS −78 °C → 45 °C, 30 min	2.4	76	0	0
B_{1-3}	$(PhCH_2OCH_2)_2CuLi$ (**8a**)	THF–DIPS, Me_3SiCl −78 °C, 15 min	2.4	85	74	19
C_{1-3}	$PhCH_2OCH_2CuCNLi$ (**9a**)	THF −78 °C → 0 °C, 30 min	1.2	25		(11)[a]
D_{1-3}	$(PhCH_2OCH_2)_2CuNLi_2$ (**10a**)	THF −78 °C → −10 °C, 15 min	2.4	55		(16)[b]
E_{1-3}[c]	$PhCH_2OCH_2Cu$ (**11a**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −45 °C, 30 min	2.0	68	66	59
F_{1-3}[c]	$PhCH_2OCH_2Cu{\cdot}(LiBr)_n$ (**12a**)	THF, $BF_3{\cdot}OEt_2$ −78 °C → −20 °C, 1 h	1.2			25
G_{1-3}[c]	$(PhCH_2OCH_2)_2CuLi$ (**8a**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −50 °C, 30 min	2.4			35
H_{1-3}[d]	$PhCH_2OCH_2Cu$ (**11a**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −50 °C, 30 min	1.2	95	51	54
I_{1-3}[d]	$PhCH_2OCH_2Cu$ (**11a**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −50 °C, 30 min	2.0			69
J_{1-3}	$(THPOCH_2)_2Cu$ (**8b**)	THF–DIPS −78 °C → −45 °C, 30 min	2.4	67		
K_{1-3}[c]	$THPOCH_2Cu$ (**11b**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −50 °C, 30 min	2.0	41	23	31
L_{1-3}[d]	$THPOCH_2Cu$ (**11b**)	THF–DIPS, $BF_3{\cdot}OEt_2$ −78 °C → −50 °C, 30 min	1.2			50

[a] Product from boron trifluoride etherate mediated reaction contaminted with 33 mol % of inseparable 1,2-bis(benzyloxy)ethane (**20a**). [b] Product from boron trifluoride etherate mediated reaction contaminated with 50 mol % of 1,2-bis(benzyloxy)ethane (**20a**). [c] The organocopper reagent was treated with boron trifluoride etherate followed by subsequent addition of the enone according to the genral procedure of Yamamoto.[21] [d] The organocopper reagent was treated with the enone followed by subsequent addition of boron trifluoride etherate (see text and Experimental Section).

reagent precursors needed in order to make applications to diastereomerically or enantiomerically defined reagents practical.

Results

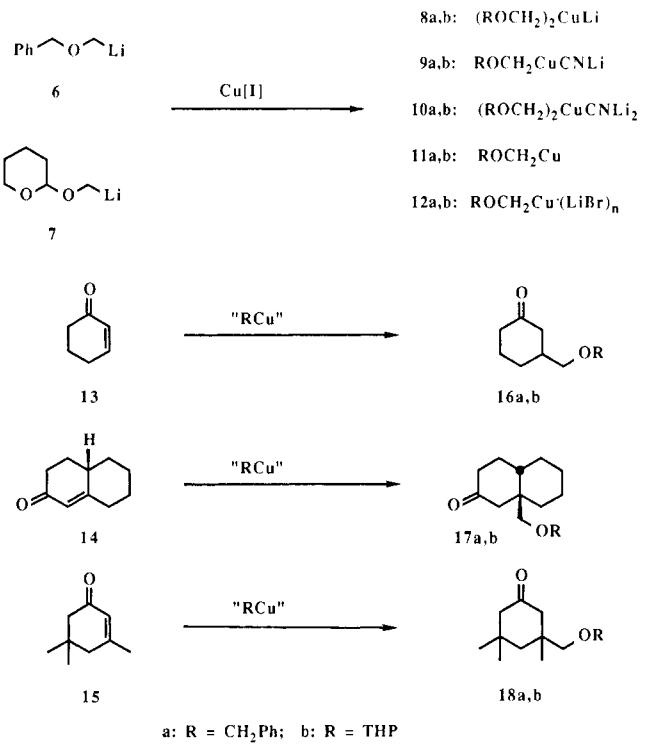
The α-alkoxystannane precursors for the lithium reagents needed in these studies were prepared from tri-*n*-butyl(iodomethyl)stannane (**1**) and the appropriate alcohols by a slight modification of the method of Still,[2b] as shown in Scheme I. Thus stannane **3** was obtained in 82% yield from benzyl alcohol (**2**), and stannane **5** was obtained in 72% yield from 2-hydroxytetrahydropyran (**4**).[10] Both stannanes **3** and **5** underwent virtually instantaneous transmetalation upon treatment with *n*-butyllithium in THF at −78 °C using the conditions described by Still,[2b] to give the yellow (α-alkoxymethyl)lithium reagents **6** and **7** as shown. Interestingly, (benzyloxy)methylstannane **3** also underwent transmetalation in diethyl ether at −78 °C to give **6**, but the transmetalation required 35–40 min to reach completion under these conditions.[11] In contrast, stannane **5** did not undergo useful levels of transmetalation in diethyl ether at −78 °C. Since lithium reagent **7** was found to be unstable at temperatures above ca. −65 °C, warming the ethereal solution of **5** and *n*-butyllithium to achieve complete transmetalation was not a viable option, and consequently the chemistry of lithium reagent **7** in diethyl ether was not further pursued. Such a pronounced solvent-dependent transmetalation rate difference is not unexpected since transmetalation reactions appear to be facilitated by better donor solvents.[12]

With the ability to prepare (α-alkoxymethyl)lithium reagents **6** and **7** under a number of different experimental conditions, conjugate addition experiments could be undertaken. As shown in Scheme II, organocopper reagents **8–12** were prepared from (α-alkoxymethyl)lithium reagents **6** and **7** and allowed to react with enones **13–15**, affording 1,4 adducts **16–18**. Results of these studies are summarized in Table I.

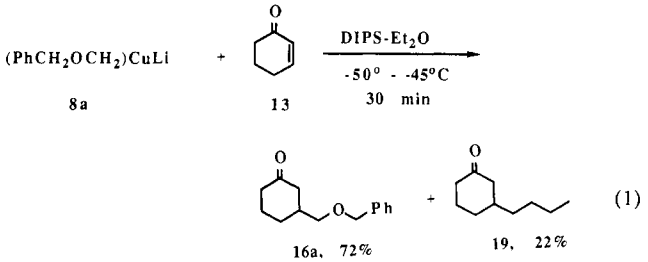
It becomes apparent from the data presented in Table I that the (α-alkoxymethyl)homocuprates **8** prepared from lithium reagents **6** and **7** and copper(I) bromide–dimethyl sulfide complex are relatively unreactive, requiring temperatures of −45 °C for successful conjugate addition to occur with cyclohex-2-en-1-one (**13**), regardless of whether THF (runs A_1 and J_1; runs given in Table I) or diethyl ether are used as the reaction solvent. Although House has unequivocally demonstrated that a number of homocuprate reagents are considerably more reactive in diethyl ether than in THF,[9b] homocuprate **8a** prepared from lithium reagent **6** generated in diethyl ether does not undergo complete reaction with cyclohex-2-en-1-one (**13**) until the reaction mixture has been

(10) Schniepp, L. E.; Geller, H. H. *J. Am. Chem. Soc.* **1946**, *68*, 1646.
(11) Schöllkopf, U. In *Houben-Weyl-Müller: Methoden der Organischen Chemie*; Thieme: Stuttgart, 1970; Vol. 13/1, p 133.
(12) See, for example: (a) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101. (b) Reich, H. J.; Phillips, N. H. *J. Am. Chem. Soc.* **1986**, *108*, 2102.

Scheme II



stirred at −50 to −45 °C for 30 min, conditions identical with those required when THF is used as reaction solvent. While **16a** is obtained in 72% yield under these conditions, this result is marred by the formation of butyl adduct **19** in 22% yield, resulting from the presence of *n*-butyllithium because of a less favorable equilibrium in the transmetalation of stannane **3**. In contrast, **19** is only formed in trace quantities (by TLC) when the reaction is run in THF. Since the transmetalation of stannane **3** was not as favorable in diethyl ether as in THF, and because lithium reagent **7** cannot be generated in diethyl ether, the use of diethyl ether as a solvent for reactions of (α-alkoxymethyl)copper reagents was not further investigated.

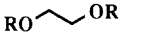


(1)

The lowered reactivity of homocuprates **8** apparently accounts for their inability to react with more hindered enones **14** and **15**, and warming reaction mixtures above −25 °C in an attempt to facilitate the reaction with these enones only resulted in the decomposition of the cuprate (runs A_2 and A_3). In contrast, activation of the homocuprate **8a** with chlorotrimethylsilane by the method of Corey and Boaz[13] afforded virtually instantaneous reaction at −78 °C with enones **13** and **14**, cleanly affording adducts **16a** and **17a** in 85% and 74% yields, respectively (runs B_1 and B_2), after mild acid hydrolysis of the intermediate trimethylsilyl enol ethers. Unfortunately, this procedure only affords marginal results in the case of the exceedingly hindered enone isophorone (**15**) where the yield of **18a** under otherwise identical reaction conditions is only 19% (run B_3), with the remainder of the product mixture consisting of unchanged isophorone.

While these results were encouraging, the use of homocuprate reagents **8** necessitates the sacrifice of 1 equiv of the (α-alkoxymethyl)lithium reagent. Consequently, it was hoped that other organocopper reagent preparations reported in the literature would allow more economical use of (α-alkoxymethyl)lithium reagents and, in the case of some of the more reactive reagent systems, provide useful results with highly hindered enones such as isophorone (**15**).

The use of lower order[14] and higher order cuprates[15] prepared from copper(I) cyanide was investigated briefly. It was quickly found that treatment of a slurry of commerical (Fisher C-461) copper(I) cyanide in THF with 1.0 equiv of lithium reagent **6** afforded no lower order cyanocuprate **9a**. Instead, only 1,2-bis(benzyloxy)ethane (**20a**)[16] resulting from dimerization of lithium reagents **6** (presumably by copper(II) impurities in the copper(I) cyanide) could be isolated.[17,18] Samples of copper(I) cyanide of considerably higher quality than commercial material could be prepared by the method of Barber,[19] and treatment of this material with lithium reagent **6** afforded both the brown-orange lower order cyanocuprate **9a** and the yellow higher order cyanocuprate **10a** after brief warming to −50 °C to effect reagent formation. Unfortunately, warming to −50 °C was necessary to effect complete dissolution of the copper(I) cyanide. While lithium reagent **6** appeared to be stable at −50 °C long enough to allow successful reagent formation, lithium reagent **7** underwent rapid thermal decomposition above −65 °C, thus precluding the preparation of reagents **9b** and **10b**.



(2)

20a: R = CH_2Ph
20b: R = THP

These reagents did not offer any advantage over homocuprates **8** in reactions with cyclohex-2-en-1-one (**13**), as shown in Table I (runs C_1 and D_1). While both reagents **9a** and **10a** were inert to isophorone (**15**), addition of boron trifluoride etherate[20] to either **9a** or **10a** prior to introduction of **15** allowed isolation of **18a** in low yield (runs C_3 and D_3). In both cases, ketone **18a** was contaminated with chromatographically inseparable 1,2-bis(benzyloxy)ethane (**20a**), indicating that, despite the higher quality of the copper(I) cyanide prepared by the method of Barber, this material was still contaminated with significant levels of copper(II) impurities. In contrast, ketone **18a** prepared from homocuprate **8a** derived from copper(I) bromide–dimethyl sulfide complex (run B_3) showed no contamination with **20a**.

More encouraging results were obtained by using the $RCu\cdot BF_3$ reagent system developed by Yamamoto.[21] Treatment of a THF solution of 2.0 equiv of ((benzyloxy)methyl)copper (**11a**) at −78 °C with 2.0 equiv of boron trifluoride etherate followed by introduction of 1.0 equiv of enones **13**–**15** afforded virtually instantaneous reaction at −78 °C to give enones **16a**–**18a** in moderate

(13) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015, 6019.

(14) (a) Prout, F. S.; Abdulslam, M. M. E. *J. Chem. Eng. Data* **1966**, *11*, 616. (b) Gorlier, J.-P.; Hamon, L.; Levisalles, J.; Wagnon, J. *J. Chem. Soc., Chem. Commun.* **1973**, 88.

(15) Lipschutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005 and references cited therein.

(16) The presence of 1,2-bis(benzyloxy)ethane (**20a**) or 1,2-bis[(tetrahydropyran-2-yl)oxy]ethane (**20b**) in crude reaction mixtures or purified products was ascertained by comparison with authentic samples of these materials. Samples of **20a** and **20b** were prepared by modifications of existing literature procedures and gave satisfactory ^1H NMR, infrared, and mass spectral data. **20a**: Normant, H.; Cuvigny, T. *Bull. Soc. Chim. Fr.* **1966**, 1866. **20b**: Woods, G. F.; Kramer, D. N. *J. Am. Chem. Soc.* **1947**, *69*, 2246.

(17) Commerical copper(I) cyanide contains 6–8% of copper(I) chloride, which conceivably could undergo oxidation. See ref 9 (Bertz, S. H., personal communication) of: Hope, H.; Oram, D.; Power, P. P. *J. Am. Chem. Soc.* **1984**, *106*, 1149.

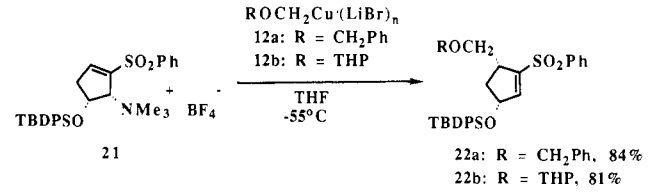
(18) For a study on dimerization of organocopper reagents using copper(II) salts and other oxidizing agents, see: Whitesides, G. M.; San Filippo, J., Jr.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302.

(19) Barber, H. J. *J. Chem. Soc.* **1943**, 79.

(20) Lipschutz, B. H.; Parker, D. A.; Kozlowski, J. A.; Nguyen, S. L. *Tetrahedron Lett.* **1984**, *25*, 5959.

(21) (a) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 3240. (b) Yamamoto, Y.; Yamamoto, S.; Yatagi, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* **1982**, *47*, 119.

Scheme III



21

22a: R = CH_2Ph, 84%
22b: R = THP, 81%

to good yields as shown in Table I (runs E_1–E_3). By comparison, slightly lower yields of ketones **16b–18b** were obtained under otherwise identical conditions by treatment of enones **13–15** with (((tetrhydropyran-2-yl)oxy)methyl)copper (**11b**) and boron trifluoride etherate (runs K_1–K_3).

While use of the Yamamoto reagent system afforded useful results with all three enones **13–15** for the first time, use of fewer than 2.0 equiv of (α-alkoxymethyl)copper reagents **11** in this procedure afforded drastically reduced yields of ketones **16–18**, an observation similar to those reported independently by other workers.[22] In hopes of finding a procedure that would require fewer equivalents of lithium reagents **6** and **7** and that would give better results with the hindered enone isophorone (**15**), a number of other variants on Yamamoto's procedure were examined. As shown in Table I, treatment of 1.2 equiv of halocuprate **12a**[23] at −78 °C with 1.2 equiv of boron trifluoride etherate followed by introduction of 1.0 equiv of isophorone (**15**) afforded only a 25% yield of **18a**, with the balance of the product mixture being unchanged isophorone (run F_3). Similarly, treatment of isophorone with homocuprate **8a** in the presence of boron trifluoride etherate according to the procedure of Smith and Jerris[24] afforded ketone **18a** in 35% yield, again with the balance of the product mixture being unchanged isophorone (run G_3).

Despite these discouraging results, a very simple modification of Yamamoto's procedure in some cases gave improved yields of conjugate addition products with use of only a slight excess of (α-alkoxymethyl)copper reagents **11**. Thus, treatment of 1.2 equiv of ((benzyloxy)methyl)copper **11a** at −78 °C with enones **13–15** followed by *subsequent* addition of boron trifluoride etherate afforded virtually instantaneous addition to give adducts **16a–18a** as shown in Table I (runs H_1–H_3). With this procedure a 95% yield of **16a** could be obtained from enone **13** (run H_1) and a 54% yield of **18a** could be obtained from isophorone (run H_3), a result which compares favorably with that obtained with 2.0 equiv of copper reagent **11a** under Yamamoto's conditions (run E_3). Application of this procedure to [((tetrahydropyran-2-yl)oxy)-methyl]copper (**11b**) and isophorone afforded ketone **18b** in 50% yield (run K_3). Finally, addition of 1.0 equiv of isophorone (**15**) to 2.0 equiv of ((benzyloxy)methyl)copper (**11a**) followed by addition of boron trifluoride etherate afforded ketone **18a** in 69% yield (run I_3), again with the balance of the product mixture being unchanged isophorone.

To further illustrate the usefulness of (α-alkoxymethyl)copper reagents, ammonium salt **21**[25] was treated with halocuprate[23a] reagents **12** under conditions used previously in a total synthesis of (+)-carbacyclin. As shown in Scheme III, halocuprate **12a** afforded cis adduct **22a** in 84% yield and halocuprate **12b** afforded cis adduct **22b** in 81% yield.

Once the utility of simpler α-alkoxycopper reagents had been demonstrated, it was decided to apply this technology to more complex substrates. Previously, Still had reported that α-alkoxylithium reagents are configurationally stable and undergo alkylation with complete retention of configuration.[2c] Similarly, Sinaÿ had shown that α- and β-D-glucosyllithium reagents are also configurationally stable and undergo alkylation with complete retention of configuration.[26] Finally, Whitesides has demonstrated that a cuprate derived from *endo*-2-norbornylmagnesium bromide[27] undergoes conjugate addition to mesityl oxide with complete retention of configuration.[28] It was thus felt that a new stereospecific synthesis of *C*-glycosides could be developed utilizing conjugate addition reactions of organocopper reagents derived from α- and β-D-glucosyllithium reagents.[29]

Table II. ^{1}H NMR Data for *C*-Glycosides **25**[a]

compd	H2β	H2α	$J_{12\beta}$	$J_{12\alpha}$	$J_{2\beta2\alpha}$	$J_{2\beta3}$	$J_{2\alpha3}$
β-**25a**	1.28	1.82	12.9	<2	11.9	12.9	4.2
α-**25a**	1.70	1.75	2.9	2.9	14.3	7.6	4.8
β-**25b**	1.39	1.95	11.5	<2	11.5	11.5	3.4

[a] Chemical shifts are given in ppm (δ) downfield from internal tetramethylsilane; coupling constants are given in hertz (Hz).

As shown in Scheme IV, stannanes β-**23a** and α-**23a** (prepared from triacetyl glucal by a modification of methods reported by Sinaÿ[26]) underwent virtually instantaneous transmetalation in THF at −78 °C upon treatment with *n*-butyllithium to afford lithium reagents β-**23b** and α-**23b**. Addition of lithium reagents β-**23b** and α-**23b** to a solution of 1.1 equiv of copper(I) bromide-dimethyl sulfide complex in 1:1 diisopropyl sulfide–THF at −78 °C afforded the brown glucosylcopper reagents β-**23c** and α-**23c**. As shown, treatment of β-**23c** with methyl vinyl ketone (**24a**) at −78 °C followed by addition of boron trifluoride etherate according to the modified Yamamoto protocol afforded β-**25a** in 55% yield. Treatment of α-**23c** with methyl vinyl ketone (**24a**) under identical conditions afforded α-**25a** in 75% yield. Examination by 470-MHz ^{1}H NMR and HPLC revealed that both glucosylcopper reagents β- and α-**23c** had undergone conjugate addition with complete retention of the configuration of the anomeric carbon and that neither isomer was contaminated with detectable levels of the other. The assignment of the configuration of the anomeric carbon in both β- and α-**25a** was confirmed by the coupling constants between the anomeric proton on C1 and the methylene protons on C2; these values are compiled in Table II without further comment except to note that they are consistent with values reported by both Sinaÿ[26] and Hannessian[30] for related systems.

The limitations of this technology became evident upon attempted reaction of glucosylcopper reagents with mesityl oxide (**24b**). Thus, treatment of copper reagent β-**23c** with mesityl oxide under the modified Yamamoto conditions produced no 1,4 addition until the reaction mixture was warmed to 0 °C. This procedure afforded a 20% yield of adduct β-**25b** as a single stereoisomer. Confirmation of the stereochemistry again was based upon ^{1}H NMR coupling constants as shown in Table II, which were in close agreement with values obtained for β-**25a**. Unfortunately, repetition of this reaction by using isomeric copper reagent α-**23c** under identical conditions also gives β-**25b** as the only product of conjugate addition in 8% yield. Clearly, at the elevated temperatures required for successful union of the secondary and tertiary centers of reagent α-**23c** and mesityl oxide (**24b**) the axial glucosylcopper reagent α-**23c** is undergoing inversion of configuration to give the more stable equatorial glucosylcopper reagent β-**23c** prior to conjugate addition.[31] Illustrative of the relatively attenuated reactivity of glucosylcopper reagents β- and α-**23c** is the observation that ((benzyloxy)methyl)copper (**11a**) undergoes

(22) (a) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047. (b) Oppolzer, W.; Löher, H. *Helv. Chim. Acta* **1981**, *64*, 2808. (c) Oppolzer, W.; Dudfield, P.; Stevenson, T.; Godel, T. *Helv. Chim. Acta* **1985**, *68*, 212. (d) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1981**, *64*, 1123.

(23) (a) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.*, in press. (b) Hutchinson, D. K.; Hardinger, S. A.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1425.

(24) Smith, A. B., III; Jerris, P. J. *J. Am. Chem. Soc.* **1981**, *103*, 194. It must be noted that these workers state that one recycle of unchanged starting material was required to achieve a 70% yield of conjugate addition products.

(25) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1985**, *107*, 6137.

(26) (a) Lancelin, J.-M.; Morin-Allory, L.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1984**, 355. (b) Lesimple, P.; Beau, J.-M.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1985**, 894.

(27) Jensen, F. R.; Nakamaye, K. L. *J. Am. Chem. Soc.* **1966**, *88*, 3437.

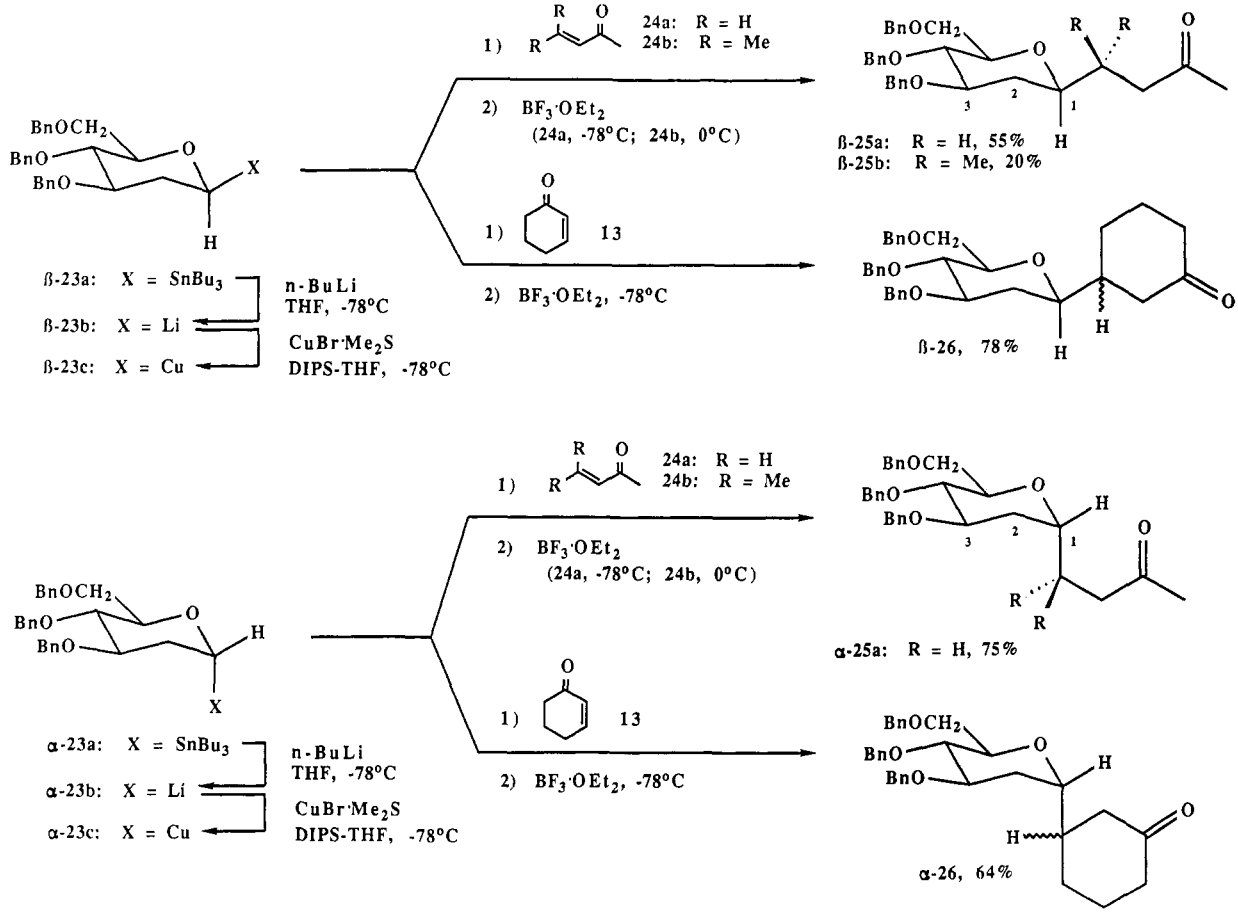
(28) Whitesides, G. M.; Kendall, P. E. *J. Org. Chem.* **1972**, *37*, 3718.

(29) Syntheses of *C*-glycosides using α-alkoxy *vinyl* anions have also been recently reported: (a) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E. *J. Chem. Soc., Chem. Commun.* **1986**, 925. (b) Hanessian, S.; Martin, M., Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926.

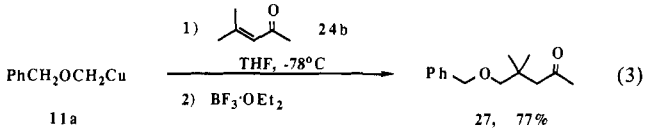
(30) Hanessian, S.; Pernet, A. G. *Can. J. Chem.* **1974**, *52*, 1266.

(31) A number of configurationally defined organocopper reagents undergo epimerization at temperatures above −78 °C, and this is especially true at ambient temperatures. For a brief discussion, see ref 4 of: Periasamy, M. P.; Walborsky, H. M. *J. Am. Chem. Soc.* **1975**, *97*, 5930.

Scheme IV



boron trifluoride promoted conjugate addition to mesityl oxide within 10 min at −78 °C under otherwise identical conditions to give **27** in 77% yield.



(3)

Fortunately, the coupling of two secondary centers is still a facile process. Thus, treatment of glucosylcopper reagent β-**23c** with cyclohex-2-en-1-one (**13**) under the modified Yamamoto conditions afforded virtually instantaneous reaction at −78 °C to afford β-**26** in 78% yield. Similar treatment of glucosylcopper reagent α-**23c** afforded α-**26** in 64% yield.

The 470-MHz ^{1}H NMR indicated that the adducts from glucosylcopper reagents β- and α-**23c** had been obtained as 1:1 mixtures of diastereomers. Due to the many overlapping resonances in the 470-MHz ^{1}H NMR, it was difficult to ascertain whether this was because epimerization of the C1 position had occurred or whether no significant level of diastereoselection had been obtained in the conjugate addition. ^{13}C NMR showed that two different mixtures of diastereomers had been obtained in the case of adducts β-**26** and α-**26** and that there was no detectable cross contamination. Significantly, the ^{13}C NMR of α-**26** showed only a single set of signals for the carbohydrate ring carbons, whereas there were two sets of peaks for carbons attributable to the cyclohexanone moiety, suggesting that no C1 isomerization had taken place. Finally, HPLC allowed separation of the diastereomeric components of β-**26** and showed unequivocally that the two sets of diastereomers obtained as β- and α-**26** were different from one another. Here, it must be noted that the conjugate addition process affording β- and α-**26** had occurred at −78 °C, conditions under which methyl vinyl ketone adducts β- and α-**25a** could be obtained diastereomerically pure. As a result of these considerations, β- and α-**26** are assigned the diastereomeric structures shown in Scheme IV, where complete retention of the configuration of the anomeric carbon had been obtained in the conjugate addition with no significant diastereoselection.

Discussion

As can be seen from the above data, given appropriate reaction conditions α-alkoxycopper reagents can be synthetically useful, giving good yields of substrates accessible otherwise only by multistep reaction sequences.[5,6] In addition, these reagents can be induced to undergo useful levels of conjugate addition even with highly hindered enones such as isophorone (**15**).

The major limitation to the use of α-alkoxycopper reagents appears to be their lack of reactivity, which necessitates activation with chlorotrimethylsilane[13] or boron trifluoride etherate[21] for successful conjugate addition to occur with enones more hindered than cyclohex-2-en-1-one (**13**). Preliminary studies suggested that this situation is not improved by the use of diethyl ether as a solvent in place of THF, and results are complicated by the fact that the equilibrium constant of the transmetalation of stannanes **3** and **5** is not as favorable in diethyl ether as it is in THF. This situation becomes even more severe in the case of the secondary glucosyl copper reagents β- and α-**23c**, which require temperatures of 0 °C for detectable reaction to occur with mesityl oxide (**24b**) even in the presence of boron trifluoride etherate, conditions under which these reagents were configurationally unstable.

It must also be noted that the quality of the copper(I) source used in the preparation of α-alkoxycopper reagents is very important to the success of their conjugate addition reactions. The majority of these experiments were performed with the very high quality copper(I) bromide-dimethyl sulfide complex prepared by the method of Townsend.[32] As an added precaution, this material was treated in situ with ca. 5 mol % of isopropylmagnesium

(32) (a) Theis, A. B.; Townsend, C. A. *Synth. Commun.* **1981**, *11*, 157. (b) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

chloride prior to introduction of the lithium reagent, to scavenge any traces of copper(II) impurities, since Grignard reagents are known to reduce copper(II) salts.[33] While the effectiveness (or necessity) of this procedure in all cases remains to be established,[34] it was observed that dimers **20a** and **20b** were not formed in levels detectable by TLC or ^{1}H NMR in reactions of α-alkoxycopper reagents prepared from copper(I) bromide–dimethyl sulfide complex that had been treated in this manner. The only time formation of 1,2-bis(benzyloxy)ethane (**20a**)[16] could be observed was when copper(I) cyanide[17,19] or copper(I) bromide–dimethyl sulfide complex that had seen 3 months of storage and handling was used for preparation of α-alkoxycopper reagents. In general, this problem could be prevented by using copper(I) bromide–dimethyl sulfide complex within 2 months of its preparation and by avoiding the use of copper(I) cyanide completely.

In addition to these considerations, because of the thermal lability of α-alkoxylithium reagents,[35] use of soluble copper(I) sources appears advantageous. Thus, use of a solution of copper(I) bromide–dimethyl sulfide complex in diisopropyl sulfide–THF[36] permits rapid formation of α-alkoxycopper reagents at −78 °C. In contrast, formation of lower order and higher order cyanocuprates **9a** and **10a** from lithium reagent **6** requires warming to −50 °C to effect complete dissolution of the insoluble copper(I) cyanide. Under similar conditions, formation of cyanocuprates from [((tetrahydropyran-2-yl)oxy)methyl]lithium **7** was completely unsuccessful due to its thermal decomposition prior to reaction with the insoluble copper(I) cyanide.

In summary, this work has examined the conjugate addition chemistry of α-alkoxycopper reagents. Experimental considerations such as purity of the copper(I) source and reactivity with enones of increasing steric demand were defined. Finally, application to the stereospecific synthesis of *C*-glycosides by conjugate addition of stereochemically defined glucosylcopper reagents was examined. In all cases, α-alkoxycopper reagents exhibited behavior typical of the more common alkylcopper reagents and allowed access to substrates which would be otherwise accessible only by multistep reaction sequences.

Experimental Section[43]

Materials. Boron trifluoride etherate was distilled with excess diethyl ether over calcium hydride by the method of Brown.[38] Diisopropyl sulfide, dimethyl sufide, and *N,N*-dimethylformamide were distilled over calcium hydride and stored over 4-Å molecular sieves under argon in a dry bottle sealed with a septum. Diethyl ether and THF were distilled over sodium–benzophenone ketyl. Chlorotrimethylsilane was purified by distillation over calcium hydride under argon into a dry (ca. 100 mL) bottle previously charged with a 1-cm layer of cross-linked poly(4-vinylpyridine) and stored under argon after careful sealing of the bottle with a septum; material so purified could be stored at ambient temperature for 30 days without detectable loss of quality.[39] Copper(I) cyanide was prepared by the method of Barber[19] and azeotropically dried with toluene in vacuo followed by storage under argon in a desiccator . Copper(I) bromide–dimethyl sulfide complex was prepared by the method of Townsend.[32] In our hands, this material melted at 127–130 °C; material having a melting range beginning at temperatures lower than 127 °C was deemed unsatisfactory for use and discarded. Material having a satisfactory melting point was stored under argon in a desiccator and was discarded after 2 months of use; older material (3–4 months) generally contained (presumably) copper(II) impurities, which resulted in the formation of detectable levels of 1,2-bis(benzyloxy)ethane (**20a**) that was chromatographically inseparable from isophorone adduct **18a**. Alkyllithium reagents were analyzed by titration of a 0.5 M solution of menthol in benzene at ambient temperature by using 2,2′-bipyridyl as an indicator.[40]

General Procedures. All reactions were performed in oven *and* flame-dried glassware under a positive pressure of argon. Absence of air and moisture was insured by alternate evacuation with an oil pump and purging with argon by means of a double-tube manifold equipped with a Firestone valve (Ace Glass Catalog No. 8766). Air- and moisture-sensitive reagents were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. A "cooled cannula" was used *in all cases* for flask-to-flask transfers of the thermally sensitive α-alkoxylithium and -copper reagents. The cooled cannula was prepared as follows: An oven-dried cannula was flushed with argon and placed with the ends through the septa of the two flasks involved in the transfer. The cannula was then cooled by the repeated rubbing of a piece of dry ice along its entire length, followed immediately by the flask-to-flask solution transfer while the piece of dry ice is held against the cannula for the complete duration of the transfer operation. The "1:1 NH_3–NH_4Cl solution" used in the workup of copper reactions was prepared by mixing equal portions of concentrated aqueous ammonium hydroxide solution and saturated aqueous ammonium chloride solution. Progress of reactions was followed by thin-layer chromatographic (TLC) analysis in comparison to starting materials. Thin-layer chromatography was performed using EM Laboratories precoated silica gel 60F-254 plates that were 0.25 mm thick. TLC plates were visualized with UV light and *p*-anisaldehyde solution[41] or 10% (w/v) phosphomolybdic acid in ethanol. Where *p*-anisaldehyde solution was used, spots were generally shades of blue or black unless otherwise noted. Gravity column chromatography was performed by using 60–200-mesh silica gel obtained from Sargent-Welch or Davison Chemical. Flash chromatography[42] was performed by using 200–400-mesh silica gel obtained from EM Laboratories. All yields refer to isolated, purified materials of >95% purity as ascertained by a combination of TLC and/or HPLC and ^{1}H and ^{13}C NMR examination.

Tributyl[((tetrahydropyran-2-yl)oxy)methyl]stannane (5). A slurry of 0.99 g (1.64 g, 60% in mineral oil, 41.1 mmol) of sodium hyride, previously washed with diethyl ether (3 × 15 mL) to remove mineral oil, in 20 mL of THF at 0 °C was treated with a solution of 3.0 g (29.4 mmol) of 2-hydroxytetrahydropyran[10] in 25 mL of THF over 15 min, the solution becoming viscous toward the end of the addition. The solution was then warmed to ambient temperature for 1 h, followed by addition of 12.65 g (29.4 mmol) of neat tributyl(iodomethyl)stannane (**1**)[2b] and washing the addition funnel with 5 mL of THF after addition of the stannane was complete. The solution was stirred at ambient temperature for 2 min, and 15 mL of DMF was added dropwise over 2 min. The solution warmed slightly during addition and was allowed to stir at ambient temperature for 48 h, followed by cooling to 0 °C and addition of 50 mL of saturated NH_4Cl over 15 min. The mixture was diluted with 50 mL of water and 200 mL of dichloromethane. The aqueous layer was extracted with dichloromethane (3 × 100 mL), and the combined organic layers were extracted with 200 mL of saturated NH_4Cl. Drying (Na_2SO_4) and concentration in vacuo afforded a yellow oil which was chromatographed over 900 g of 60–200-mesh silica gel eluting with 4000 mL

(33) Wada, K.; Tamura, M.; Kochi, J. *J. Am. Chem. Soc.* **1970**, *92*, 6656.
(34) This procedure is, however, very effective in the reduction of traces of copper(II) impurities (as evidenced by a yellow color which disappears completely, giving a colorless solution upon addition of the Grignard reagent) of THF solutions of Li_2CuBr_4 (from 1.0 equiv of copper(I) bromide–dimethyl sulfide complex and 3.0 equiv of lithium bromide) used in preparation of halocuprates **12** (see Experimental Section).[23] Also see: Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.
(35) For studies on the decomposition of α-alkoxylithium reagents, see: (a) Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763. (b) Garst, J. F.; Smith, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 1526. (c) Lansbury, P. T.; Pattison, J. T.; Sidler, J. D.; Bieker, J. B. *J. Am. Chem. Soc.* **1966**, *88*, 78. (d) Schafer, H.; Schöllkopf, U.; Walker, D. *Tetrahedron Lett.* **1968**, *9*, 2809. (e) Ziegler, V. K.; Geelect, H. G. *Liebigs Ann. Chem.* **1950**, *567*, 185. (f) Peterson, D. J. *Organomet. Chem. Rev. A* **1972**, *7*, 295.
(36) Corey, E. J.; Carney, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 7318.
(37) Patt, S. L.; Shoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.
(38) Zweifel, G.; Brown, H. C. *Org. React.* **1963**, *13*, 28.
(39) Hutchinson, D. K. *Aldrichimica Acta* **1986**, *19*, 58.
(40) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9* 165.
(41) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 379.
(42) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(43) **Analytical.** All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected, as are boiling points. Infrared spectra were determined by using a Perkin-Elmer 1420 grating spectrophotometer, neat or in chloroform solution. Characteristic absorption maxima are reported in both wave numbers (cm^{-1}) and microns (μm). ^{1}H NMR spectra were determined on a Perkin-Elmer R32 (90 MHz) or a Nicolet NT 470 (470 MHz) spectrometer. Spectra were determined in chloroform-*d* or benzene-d_6 as noted, and chemical shifts are reported in parts per million (ppm, δ) downfield from internal tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, o = overlapping), integration, coupling constant (Hz), and interpretation. ^{13}C NMR spectra were determined on a Varian XL-200 (50 MHz). Broad-band-decoupled and APT[37] spectra are reported. Spectra were determined in chloroform-*d* and are referenced to the center line of the triplet at 77.00 ppm. APT spectra are assigned an o (odd) for carbons with one or three attached hydrogen atoms and an e (even) for carbons with zero or two attached hydrogen atoms. Low-resolution mass spectra were determined on a Finnegan 4000 instrument with a Nova 4 data system at 70 eV. High-resolution mass spectra were determined on a Kratos MS 50 instrument at 70 eV. In general, exact masses were determined on the molecular ion in the EI or CI mode or alternatively on the highest mass fragment ion having a relative abundance of 10% or greater, as noted.

of hexane and then with 3% (v/v) ethyl acetate in hexane. These procedures afforded 8.59 g (72%) of stannane **5** as a heavy, colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.56; ^{1}H NMR ($CDCl_3$) δ 4.48 (m, 1 H, H2 of THP), 4.2–3.3 (m, 2 H, H6 of THP), 4.08, 3.66 (AB, 2 H, J_{gem} = 11.2 Hz, OCH_2Sn), 2.0–0.7 (om, 31 H); IR (neat) cm^{-1} (μm) 2900 (3.4), 1460 (6.8), 1375 (7.3), 1195 (8.4), 1120 (8.9), 1075 (9.3), 1015 (9.9), 960 (10.4), 900 (11.1), 870 (11.5); mass spectrum (EI), m/z (rel intensity) 349 ($M^+ - C_4H_9$, 61), 291 (22), 235 (22), 177 (31), 85 (100).

Exact mass (EI) calcd for $C_{14}H_{29}O_2Sn$ ($M^+ - C_4H_9$) 349.1182, found 349.1192.

3-((Benzyloxy)methyl)cyclohexan-1-one (16a) from ((Benzyloxy)methyl)copper (11a) and Boron Trifluoride Etherate by Modified Yamamoto Protocol (Run H_1). A solution of 322 mg (1.565 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.5 mL of diisopropyl sulfide and 1.6 mL of THF at −78 °C was treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF, followed by stirring at −78 °C for 20 min. A solution of 585 mg (1.423 mmol) of stannane **3** in 7.0 mL of THF was treated with 0.58 mL (2.49 M, 1.451 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to the copper(I) bromide solution followed by stirring at −78 °C for 15 min. The brown homogeneous solution was treated with 114 mg (115 μL; 1.186 mmol) of neat cyclohex-2-en-1-one (**13**) followed by stirring at −78 °C for 5 min and addition of 222 mg (192 μL, 1.565 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 15 min, followed by warming to 0 °C for 3 min and addition to 50 mL of 1:1 NH_3–NH_4Cl solution. The mixture was diluted with 30 mL of dichloromethane and stirred at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4). Concentration in vacuo afforded a colorless oil which was chromatographed over 20 g of 200–400-mesh silica gel eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 10% (v/v) ethyl acetate in hexane. These procedures afforded 247 mg (95%) of **16a** as a colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.28; ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 5 H, Ph), 4.48 (s, 2 H, CH_2Ph), 3.37 (d, 2 H, J = 4.6 Hz, CH_2OCH_2Ph), 2.6–1.3 (om, 9 H); ^{13}C NMR ($CDCl_3$) δ 211.29 (e, C=O), 138.21 (e, Ph), 128.37 (o, Ph), 128.29 (o, Ph), 127.50 (o, Ph), 127.41 (o, Ph), 74.11 (e, OCH_2Ph), 73.00 (e, CH_2OCH_2Ph), 44.75 (e), 41.34 (e), 39.17 (o, C3), 28.08 (e), 24.87 (e); IR (neat) cm^{-1} (μm) 3060 (3.3), 2900 (3.4), 1710 (5.8), 1495 (6.7), 1450 (6.9), 1420 (7.0), 1360 (7.4), 1315 (7.6), 1220 (8.1), 1100 (9.1), 740 (13.5), 695 (14.4); mass spectrum (EI), m/z (rel intensity) 218 (M^+, 2), 127 (6), 97 (60), 91 (100).

Exact Mass (CI) calcd for $C_{14}H_{19}O_2$(M + H) 219.1380, found 219.1369.

3-[((Tetrahydropyran-2′-yl)oxy)methyl]cyclohexan-1-one (16b) from Homocuprate 8b (Run J_1). A solution of 511 mg (1.812 mmol) of stannane **5** in 9 mL of THF at −78 °C was treated with 0.77 mL (2.41 M, 1.867 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The faint-yellow solution was transferred via a cooled cannula to a solution of 205 mg (0.997 mmol) of copper (I) bromide–dimethyl sulfide complex in 1.5 mL of diisopropyl sulfide and 1.0 mL of THF at −78 °C, which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The dark-brown homogeneous solution was treated with 87 mg (88 μL, 0.906 mmol) of neat cyclohex-2-en-1-one (**13**), followed by stirring at −78 °C for 30 min and by warming to −45 to −50 °C for 1 h. The solution was then added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 1 h. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford 440 mg of a light-yellow oil. This material was chromatographed over 22 g of 200–400-mesh silica gel, eluting with 200 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 12% (v/v) ethyl acetate in hexane. These procedures afforded 128 mg (67%) of **16b** as a colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.18 (purple spot with *p*-anisaldehyde solution); ^{1}H NMR ($CDCl_3$) δ 4.66 (brs, 1 H, H2′), 4.1–3.25 (om, 4 H, H6′ and CH_2OTHP), 2.65–1.30 (om, 14 H); IR (neat) cm^{-1} (μm) 2940 (3.4), 2870 (3.5), 1710 (5.8), 1450 (6.9), 1345 (7.4), 1260 (7.9), 1200 (8.3), 1130 (8.8), 1065 (9.4), 1030 (9.7), 975 (10.3), 905 (11.1), 870 (11.5), 810 (12.3); mass spectrum (EI), m/z (rel intensity) 213 (M + H, 3), 85 (100), 67 (11), 55 (45).

Exact mass (CI) calcd for $C_{12}H_{21}O_3$ (M + H) 213.1490, found 213.1553.

***rel*-(4a*S*,8a*S*)-8a-((Benzyloxy)methyl)-1,4,4a,5,6,7,8,8a-octahydro-2(3*H*)-naphthalenone (17a) from Homocuprate 8a and Chlorotrimethylsilane (Run B_2).** A solution of 1.051 g (2.556 mmol) of stannane **3** in 12.8 mL of THF at −78 °C was treated with 1.05 mL (2.49 M, 2.607 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a solution of 276 mg (1.341 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.5 mL of diisopropyl sulfide and 1.8 mL of THF at −78 °C, which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 694 mg (0.811 mL, 6.390 mmol) of chlorotrimethylsilane,[39] followed by addition via cannula of a solution of 160 mg (1.065 mmol) of enone **14** in 2.0 mL of THF at −78 °C. The solution was stirred at −78 °C for 15 min, followed by warming to −40 °C for 10 min. The solution was warmed to 0 °C for 2 min and added to 50 mL of 1:1 NH_3–NH_4Cl solution, followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were concentrated in vacuo. The residue was dissolved in 30 mL of THF and stirred with 15 mL of 5% HCl solution at ambient temperature for 10 min. The mixture was diluted with 50 mL of dichloromethane and 30 mL of water. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a yellow oil which was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. These procedures afforded 216 mg (74%) of ketone **17a** as a colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.34; ^{1}H NMR ($CDCl_3$) δ 7.38 (s, 5 H, Ph), 4.49 (s, 2 H, CH_2Ph), 3.30, 3.20 (AB, 2 H, J_{gem} = 9.2 Hz, CH_2OCH_2Ph), 2.47 (d, 1 H, J_{gem} = 14.8 Hz, H1-eq), 2.3–2.1 (m, 1 H, H3-eq), 2.09 (d, 1 H, J_{gem} = 14.8 Hz, H1-ax), 2.0–1.2 (om, 12 H); ^{13}C NMR ($CDCl_3$) δ 212.32 (e, C=O, C2), 138.34 (e, Ph), 128.16 (o, Ph), 127.32 (o, Ph), 127.22 (o, Ph), 77.00 (e, OCH_2Ph), 73.23 (e, CH_2OCH_2Ph), 45.29 (e), 37.69 (e, C8a), 35.35 (e), 32.33 (o, C4), 27.83 (e), 26.92 (e), 24.23 (e), 21.46 (e); IR (neat) cm^{-1} (μm) 3060 (3.3), 2930 (3.4), 2860, (3.5), 1710 (5.8), 1450 (6.9), 1360 (7.4), 1230 (8.1), 1100 (9.1), 1025 (9.8), 735 (13.6), 695 (14.4); mass spectrum (EI), m/z (rel intensity) 273 (M + H, 1), 151 (100), 91 (52).

Exact mass (CI) calcd for $C_{18}H_{25}O_2$ (M + H) 273.1854, found 273.1866.

***rel*-(4a*S*,8a*S*)-8a-[((Tetrahydropyran-2′-yl)oxy)methyl]-1,4,4a,5,6,7,8,8a-octahydro-2(3*H*)-naphthalenone (17b).** A solution of 516 mg (1.274 mmol) of stannane **5** in 6.5 mL of THF at −78 °C was treated with 0.53 mL (2.49 M, 1.312 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The faint-yellow solution was transferred via a cooled cannula to a solution of 288 mg (1.401 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.4 mL of diisopropyl sulfide and 1.5 mL of THF at −78 °C, which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was then treated with 199 mg (172 μL, 1.401 mmol) of boron trifluoride etherate followed by stirring at −78 °C and addition via cannula of a solution of 96 mg (0.637 mmol) of enone **14** in 1.0 mL of THF at −78 °C. The solution was stirred at −78 °C for 5 min, followed by warming to −50 °C for 10 min, to −30 °C for 10 min, and then to 0 °C for 5 min. The solution was added to 50 mL of NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a yellow oil which was chromatographed over 25 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. The procedures afforded 45 mg of an oil which was an inseparable 7.4:1 mixture (by ^{1}H NMR integration) of ketone **17b** and starting enone **14**, this corresponding to 39 mg (23%) of **17b**: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.20 (brown–green spot with *p*-anisaldehyde solution); ^{1}H NMR ($CDCl_3$) δ 5.85 (brs, H1 of **14**), 4.53 (brs, 1 H, H2′), 3.95–2.95 (om, 4 H, H6′ of THP and CH_2OTHP), 2.55–1.20 (om, 21 H); IR (neat) cm^{-1} (μm) 2930 (3.4), 2860 (3.5), 1710 (5.8), 1675 (6.0, C=O of **14**), 1450 (6.9), 1350 (7.4), 1200 (8.3), 1125 (8.9), 1065 (9.4), 1030 (9.7), 975 (9.5), 905 (11.0), 870 (11.5), 815 (12.3).

3-((Benzyloxy)methyl)-3,5,5-trimethylcyclohexan-1-one (18a) from Cyanocuprate 9a and Boron Trifluoride Etherate (Run C_3). A solution of 465 mg (1.131 mmol) of stannane **3** in 5.6 mL of THF at −78 °C was treated with 0.47 mL (2.49 M, 1.65 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a slurry of 111 mg (1.243 mmol) of copper(I) cyanide [previously dried by azeotroping in vacuo (ca. 4 mmHg) with toluene (3 × 1.0 mL)] in 2.4 mL of THF at −78 °C. The mixture was warmed to −55 °C for 15 min. The orange-brown solution was cooled to −78 °C, and 176 mg (153 μL, 1.243 mmol) of boron

trifluoride etherate was added, followed by stirring at −78 °C for 2 min and addition of 130 mg (141 μL, 0.943 mmol) of neat isophorone (**15**). The solution was stirred at −78 °C for 10 min, followed by warming to −50 °C for 10 min and then to 0 °C over 15 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution and diluted with 30 mL of dichloromethane, followed by stirring at ambient temperature for 1 h. The aqueous phase was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL 5% (v/v) ethyl acetate in hexane and then with 8% (v/v) ethyl acetate in hexane. These procedures afforded [after pumping the sample at 4 mmHg for 18 h to remove recovered isophorone (**15**)] 41 mg of a 2:1 mixture (by ^1H NMR integration) of **18a** and 1,2-bis(benzyloxy)ethane (**20a**), this corresponding to an 11% yield of **18a**.

18a from Higher Order Cyanocuprate 10a and Boron Trifluoride Etherate (Run C_3). A solution of 664 mg (1.615 mmol) of stannane **3** in 8.0 mL of THF at −78 °C was treated with 0.67 mL (2.49 M, 1.663 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a slurry of 80 mg (0.888 mmol) of copper(I) cyanide [previously dried by azeotroping in vacuo (ca. 4 mmHg) with toluene (3 × 1.0 mL)] in 2.0 mL of THF at −78 °C. The mixture was warmed to −55 °C for 10 min. The pale-yellow solution was cooled to −78 °C, and 126 mg (109 μL, 0.888 mmol) of boron trifluoride etherate was added, followed by stirring at −78 °C for 2 min and addition of 93 mg (101 μL, 0.673 mmol) of neat isophorone (**15**), which immediately imparted a bright-yellow color to the solution. The solution was stirred at −78 °C for 10 min followed by warming to −50 °C for 10 min, to −40 °C for 10 min, and to 0 °C for 5 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl and diluted with 30 mL of dichloromethane followed by stirring at ambient temperature for 1.5 h. The aqueous phase was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a faint-yellow oil. This material was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. These procedures afforded [after pumping the sample at 4 mmHg for 18 h to remove recovered isophorone (**15**)] 55 mg of a 1:1 mixture (by ^1H NMR integration) of **18a** and 1,2-bis(benzyloxy)ethane (**20a**), this corresponding to a 16% yield of **18a**.

18a from 2.0 equiv of ((Benzyloxy)methyl)copper (11a) and Boron Trifluoride Etherate by Modified Yamamoto Protocol (Run I_3). A solution of 559 mg (1.360 mmol) of stannane **3** in 7.0 mL of THF at −78 °C was treated with 0.562 mL (2.49 M, 1.400 mmol) of *n*-butyllithium in hexane, followed by stirring at −78 °C for 10 min. The yellow solution was transferred via cooled cannula to a solution of 307 mg (1.495 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.5 mL of diisopropyl sulfide and 1.6 mL of THF at −78 °C, which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 85 mg (93 μL, 0.618 mmol) of neat isophorone (**15**), followed by stirring at −78 °C for 3 min and addition of 212 mg (0.184 mL, 1.495 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 10 min, followed by warming to −45 °C for 15 min and then to 0 °C for 10 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 16 g of 200–400-mesh silica gel, eluting the 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. These procedures afforded **18a** contaminated with unchanged isophorone (**15**); pumping on sample at 4 mmHg for 18 h at ambient temperature provided 111 mg (69%) of **18a** as a heavy oil.

18a: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.29; ^1H NMR ($CDCl_3$) δ 7.45 (s, 5 H, Ph), 4.56 (s, 2 H, CH_2Ph), 3.17 (s, 2 H, CH_2OCH_2Ph), 2.6–1.3 (om, 6 H), 1.05 (s, 9 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 212.10 (e, C=O), 138.29 (e, Ph), 128.20 (o, Ph), 127.37 (o, Ph), 127.29 (o, Ph), 79.26 (e, OCH_2Ph), 73.06 (e, CH_2OCH_2Ph), 53.82 (e), 49.00 (e), 45.82 (e), 39.69 (e, C3), 35.45 (e, C5), 32.35 (o, CH_3), 30.14 (o, CH_3), 25.91 (o, CH_3); IR (neat) cm^{-1} (μm) 3060 (3.3), 2900 (3.4), 1710 (5.8), 1450 (6.9), 1360 (7.3), 1275 (7.8), 1215 (8.2), 1100 (9.1), 735 (13.6), 695 (14.4); mass spectrum (EI), *m/z* (rel intensity) 261 (M^+, <1), 139 (100), 91 (83), 83 (45), 55 (50).

Exact mass (CI) calcd for $C_{17}H_{25}O_2$ (M + H) 261.1854, found 261.1870.

3,3,5-Trimethyl-3-[((tetrahydropyran-2′-yl)oxy)methyl]cyclohexan-1-one (18b) from (((Tetrahydropyran-2-yl)oxy)methyl)copper (11b) and Boron Trifluoride Etherate by Modified Yamamoto Protocol (Run L_3). A solution of 645 mg (1.592 mmol) of stannane **5** in 8.0 mL of THF at −78 °C was treated with 0.66 mL (2.49 M, 1.640 mmol) of *n*-butyllithium in hexane, followed by stirring at −78 °C for 10 min. The faint-yellow solution was transferred via a cooled cannula to a solution of 360 mg (1.751 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.7 mL of diisopropyl sulfide and 1.8 mL of THF at −78 °C, which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 183 mg (199 μL, 1.327 mmol) of neat isophorone (**15**) followed by stirring at −78 °C for 2 min and addition of 249 mg (215 μL, 1.751 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 10 min, followed by warming to −50 °C for 15 min and to 0 °C for 2 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 40 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. These procedures afforded **18b** contaminated with isophorone (**15**); pumping on sample at 4 mmHg for 18 h at ambient temperature provided 170 mg (50%) of **18b** as a colorless oil free of isophorone: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.36 (brown spot with *p*-anisaldehyde solution); ^1H NMR ($CDCl_3$) δ 4.63 (brs, 1 H, H2′), 3.83 (m, 1 H, H6′), 3.53 (m, 1 H, H6′), 3.53, 3.05 (overlapping AB, 2H, J_{gem} = 9.7 Hz, CH_2OTHP), 2.65–1.20 (om, 12 H), 1.06 (s, 9 H, CH_3); IR (neat) cm^{-1} (μm) 2920 (3.4), 1710 (5.8), 1450 (6.9), 1365 (7.3), 1280 (7.8), 1200 (8.3), 1125 (8.9), 1065 (9.4), 1030 (9.7), 980 (10.2), 905 (11.0), 870 (11.5), 815 (12.3); mass spectrum (CI), *m/z* (rel intensity) 255 (M + H, 100), 171 (60), 85 (26).

Exact mass (CI) calcd for $C_{15}H_{27}O_3$ (M + H) 255.1960, found 255.1955.

***rel*-(1*R*,4*R*)-*cis*-1-((Benzyloxy)methyl)-4-((*tert*-butyldiphenylsilyl)oxy)-2-(phenylsulfonyl)-2-cyclopentene (22a).** A solution of 206 mg (1.003 mmol) of copper(I) bromide–dimethyl sulfide complex and 261 mg (3.009 mmol) of LiBr in 2 mL of THF at −78 °C was treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF to remove the faint-yellow color of the solution resulting from the presence of trace levels of copper(II) impurities. The *colorless* and homogeneous solution so obtained was then stirred at −78 °C for 15 min prior to further operations. A solution of 375 mg (0.912 mmol) of stannane **3** in 4.6 mL of THF at −78 °C was treated with 0.38 mL (2.49 M, 0.939 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min and transfer via a cooled cannula to the copper(I) bromide solution previously prepared. The yellow-orange solution was stirred at −78 °C for 15 min and transferred via a cooled cannula to a slurry of 277 mg (0.455 mmol) of ammonium salt **21** in 2.0 mL of THF at −78 °C, followed by warming to −55 °C for 15 min. The homogeneous solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil. This material was chromatographed over 30 g of 200–400-mesh silica gel, eluting with 200 mL of hexane and thereafter with 7% (v/v) ethyl acetate in hexane. These procedures afforded 232 mg (87%) of **22a** as a heavy colorless oil: TLC [20%(v/v) ethyl acetate in hexane] R_f 0.27; ^1H NMR ($CDCl_3$) δ 7.85–7.25 (om, 20 H, Ph), 6.58 (dd, 1H, J_{13} = 1.8 J_{34} = 2.2 Hz, H3), 4.80 (m, 1 H, J_{34} = 2.2, $J_{45\beta}$ = 7.4, $J_{45\alpha}$ = 4.4 Hz, H4), 4.43, 4.39 (AB, 2 H, J_{gem} = 11.9 Hz, OCH_2Ph), 3.82 (dd, 1 H, J_{gem} = 9.2, $J_{11\beta'}$ = 3.8 Hz, H1β′), 3.48 (dd, 1 H, J_{gem} = 9.2, $J_{11\alpha'}$ = 8.4 Hz, H1α′), 2.96 (m, 1 H, $J_{11\beta'}$ = 3.8, $J_{11\alpha'}$ = 8.4, J_{13} = 1.8, $J_{15\beta}$ = 7.7, $J_{15\alpha}$ = 4.9 Hz, H1), 2.34 (ddd, 1 H, J_{gem} = 13.9, $J_{15\beta}$ = 7.7, $J_{45\beta}$ = 7.4, H5β), 2.09 (ddd, 1 H, J_{gem} = 13.9, $J_{15\alpha}$ = 4.9, $J_{45\alpha}$ = 4.4 Hz, H5α), 1.08 (s, 9 H, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 146.75 (e, C2), 145.40 (o, C3), 139.53 (e, Ph), 138.06 (e, Ph), 135.58 (o, Ph), 135.53 (o, Ph), 133.39 (o, Ph), 133.34 (e, Ph), 133.13 (e, Ph), 129.83 (o, Ph), 129.01 (o, Ph), 128.22 (o, Ph), 127.80 (o, Ph), 127.70 (o, Ph), 127.48 (o, Ph), 75.24 (o, C4), 72.85 (e, CH_2Ph), 71.68 (e, C1′), 43.65 (e, C5), 38.62 (o, C1), 26.71 (o, $C(CH_3)_3$), 18.97 (e, $C(CH_3)_3$); IR (neat) cm^{-1} (μm) 3070 (3.3), 2940 (3.4), 2860 (3.5), 1685 (5.9), 1460 (6.8), 1425 (7.0), 1360 (7.4), 1310 (7.6), 1150 (8.7), 1105 (9.0), 910 (11.0), 820 (12.2), 735 (13.6), 700 (14.3); mass spectrum (EI), *m/z* (rel intensity) 357 (55), 199 (24), 91 (100).

Exact mass (EI) calcd for $C_{18}H_{17}O_4SSi$ ($M^+ - C_4H_9 - C_6H_5 - C_7H_7$) 357.0617, found 357.0615.

***rel*-(1*R*,4*R*)-*cis*-4-((*tert*-Butyldiphenylsilyl)oxy)-2-(phenylsulfonyl)-1-[((tetrahydropyran-2′-yl)oxy)methyl]-2-cyclopentene (22b).** A solution of 301 mg (0.744 mmol) of stannane **5** in 3.8 mL of THF at

−78 °C was treated with 0.32 mL (2.41 M, 0.766 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The faint-yellow solution was transferred via a cooled cannula to a solution of 168 mg (0.818 mmol) of copper(I) bromide–dimethyl sulfide complex and 213 mg (2.455 mmol) of lithium bromide in 1.6 mL of THF, which has been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The yellow solution was transferred via a cooled cannula to a slurry of 226 mg (0.372 mmol) of ammonium salt **21** in 2.0 mL of THF at −78 °C. The mixture was stirred at −78 °C for 5 min, followed by warming to −55 °C for 30 min. The homogeneous yellow solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 25 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 50 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford 300 mg of an amber oil. This material was chromatographed over 18 g of 200–400-mesh silica gel, eluting with 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 12% (v/v) ethyl acetate in hexane. These procedures afforded 181 mg (85%) of **22b** as a heavy colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.23 (gray-green spot with *p*-anisaldehyde solution); ^{1}H NMR ($CDCl_3$) δ 7.9–7.4 (om, 15 H, Ph), 6.46 (dd, 1 H, J_{13} = 1.7, J_{34} = 1.7 Hz, H3), 4.76 (m, 1 H, J_{34} = 1.7, $J_{45\beta}$ = 7.0, $J_{45\alpha}$ = 4.4 Hz, H4), 4.58 (m, 1 H, H2′ of THP), 3.85–3.70 (om, 3 H, H6′ of THP and CH_2OTHP), 3.46 (m, 1 H, H6′ of THP), 2.92 (m, 1 H, J_{13} = 1.7, $J_{15\beta}$ = 7.0, $J_{15\alpha}$ = 4.4 Hz, H1), 2.31 (ddd, 1 H, J_{gem} = 13.6, $J_{15\beta}$ = 7.0, $J_{45\beta}$ = 7.0 Hz, H5β), 2.01 (ddd, 1 H, J_{gem} = 13.6, $J_{15\alpha}$ = 4.4, $J_{45\alpha}$ = 4.4 Hz, H5α), 1.85–1.45 (om, 6 H, THP), 1.04 (s, 9 H, t-Bu); IR (neat) cm^{-1} (μm) 3060 (3.3), 2900 (3.4), 1585 (6.3), 1450 (6.9), 1350 (7.4), 1310 (7.6), 1100 (9.1), 900 (11.1), 820 (12.2), 720 (13.9); mass spectrum (EI), *m/z* (rel intensity) 405 (2), 357 (14), 199 (28), 85 (100).

Exact mass (EI) calcd for $C_{18}H_{17}O_4SSi$ ($M^+ - C_4H_9 - C_6H_5 - C_5H_9O$) 357.0617, found 357.0615.

HPLC Conditions Used for Analysis of *C*-Glycosides. A 10-cm × 4.6-mm hypersil ODS (5-μm) column was used with 20% (v/v) methanol in water as a mobile phase with UV detection at 254 nm. Retention times in minutes under these conditions are given for each *C*-glycoside in the following experimental procedures: The retention time for the anomeric isomer is also given in parenthesis for comparison. Confirmation of lack of isomeric cross-contamination was obtained in each case by coinjection of a sample of the opposite anomeric isomer. In the case of cyclohex-2-en-1-one (**13**) adducts β-**26** and α-**26**, when the two diastereomers were separable, the retention time of each is given.

1-(3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-β-D-glucopyranosyl)butan-3-one (β-25a). A solution of 316 mg (0.446 mmol) of stannane β-**23a** in 2.2 mL of THF at −78 °C was treated with 0.18 mL (2.49 M, 0.456 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a solution of 101 mg (0.491 mmol) of copper(I) bromide–dimethyl sulfide complex in 0.5 mL of diisopropyl sulfide and 0.6 mL of THF at −78 °C which had been treated with one drop (10 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 26 mg (31 μL, 0.372 mmol) of neat methyl vinyl ketone (**24a**), followed by stirring at −78 °C for 2 min and addition of 70 mg (60 μL, 0.491 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 10 min, followed by warming to −50 °C for 5 min and to 0 °C for 2 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane, and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 12 g of 200–400-mesh silica gel, eluting with 100 mL of 10% (v/v) ethyl acetate and thereafter with 16% (v/v) ethyl acetate in hexane. These procedures afforded 100 mg (55%) of *C*-glycoside β-**25a** as a colorless oil: HPLC retention time = 8.01 min (α-**25a**, 7.10 min); TLC [20% (v/v) ethyl acetate in hexane] R_f 0.08 (purple spot with *p*-anisaldehyde solution); ^{1}H NMR (C_6D_6) δ 7.32–7.07 (om, 15 H, Ph), 4.97 (d, 1 H, J_{gem} = 11.1 Hz, CH_2Ph), 4.59 (d, 1 H, J_{gem} = 11.4 Hz, CH_2Ph), 4.51 (d, 1 H, J_{gem} = 11.9 Hz, CH_2Ph), 4.47–4.39 (od, 3 H, CH_2Ph), 3.69 (m, 2 H, H6′), 3.50 (m, 2 H, $J_{2\beta'3'}$ = 12.9, $J_{2\alpha'3'}$ = 4.2, $J_{3',4'}$ = 7.6, $J_{4'5'}$ = 9.5 Hz, H3′, H4′), 3.30 (7, 1 H, $J_{4'5'}$ = 9.5 Hz, H5′), 3.05 (m, 1 H, $J_{1'2\beta'}$ = 12.9, $J_{1'2\alpha'}$ = <2 Hz, H1′), 2.22 (m, 2 H, J_{gem} = 17.1 Hz, H2), 1.82 (ddd, 1 H, J_{gem} = 11.9, $J_{1'2\alpha'}$ = <2, $J_{2\alpha'3'}$ = 4.2 Hz, H2α′), 1.71 (s, 3 H, H4), 1.65 (m, 2 H, H1), 1.28 (ddd, 1 H, J_{gem} = 11.9, $J_{1'2\beta'}$ = 12.9, $J_{2\beta'3'}$ = 12.9 Hz, H2β′); ^{13}C NMR ($CDCl_3$) δ 208.46 (e, C3), 138.48 (e, Ph), 138.43 (e, Ph), 138.26 (e, Ph), 128.26 (o, Ph), 128.20 (o, Ph), 127.84 (o, Ph), 127.61 (o, Ph), 127.50 (o, Ph), 127.44 (o, Ph), 80.89 (o), 78.76 (o), 78.44 (o), 74.82 (e, CH_2Ph), 74.34 (o), 73.25 (e, CH_2Ph), 71.28 (e, CH_2Ph), 69.54 (e, C6′), 39.52 (e, C2′), 36.88 (e, C2), 29.88 (e, C1), 29.28 (o, C4); IR (neat) cm^{-1} (μm) 3025 (3.3), 2920 (3.4), 2860 (3.5), 1712 (5.8), 1495 (6.7), 1450 (6.9), 1360 (7.4), 1100 (9.1), 740 (13.5), 695 (14.4); mass spectrum (CI), *m/z* (rel intensity) 409 (M + H, 100).

Exact mass (CI) calcd for $C_{31}H_{37}O_5$ (M + H) 489.2641, found 489.2663.

1-(3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)butan-3-one (α-25a). A solution of 180 mg (0.254 mmol) of stannane α-**23a** in 1.2 mL of THF at −78 °C was treated with 0.11 mL (2.49 M, 0.262 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow-green solution was transferred via a cooled cannula to a solution of 58 mg (0.279 mmol) of copper(I) bromide–dimethyl sulfide complex in 0.5 mL of diisopropyl sulfide and 0.6 mL of THF at −78 °C which had been treated with one drop (10 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 15 mg (18 μL, 0.212 mmol) of neat methyl vinyl ketone (**24a**), followed by stirring at −78 °C for 2 min and addition of 40 mg (34 μL, 0.279 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 15 min, followed by warming to −50 °C for 10 min and to 0 °C for 3 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 14 g of 200–400-mesh silica gel, eluting with 300 mL of 10% (v/v) ethyl acetate in hexane and thereafter with 16% (v/v) ethyl acetate in hexane. These procedures afforded 78 mg (75%) of *C*-glycoside α-**25a** as a colorless oil: HPLC retention time = 7.10 min (β-**25a**, 8.01 min); TLC [20% (v/v) ethyl acetate in hexane] R_f 0.08 (purple-pink spot with *p*-anisaldehyde solution); ^{1}H NMR (C_6D_6) δ 7.28–7.08 (om, 15 H, Ph), 4.74 (d, 1 H, J_{gem} = 11.5 Hz, CH_2Ph), 4.51 (d, 1 H, J_{gem} = 11.5 Hz, CH_2Ph), 4.45–4.34 (od, 4 H, CH_2Ph), 3.82 (om, 2 H, $J_{1'2'\beta}$ = 2.9, $J_{1'2\alpha'}$ = 2.9 Hz, H1′, H6′), 3.75–3.65 (om, 3 H, $J_{2\beta'3'}$= 7.6, $J_{2\alpha'3'}$ = 4.8 Hz, H3′, H5′, H6′), 3.51 (m, 1 H, $J_{3'4'}$ = $J_{4'5}$ = 7.6 Hz, H4′), 2.21 (m, 1 H, H2), 1.84 (m, 1 H, H1), 1.75 (ddd, 1 H, J_{gem} = 14.3, $J_{1'2\alpha'}$ = 2.9, $J_{2\alpha'3'}$ = 4.8 Hz, H2α′), 1.71 (s, 3 H, H4), 1.70 (ddd, 1 H, J_{gem} = 14.3 Hz, $J_{1'2\beta'}$ = 2.9, $J_{2\beta'3'}$ = 7.6 Hz, H2β′), 1.51 (m, 1 H, H1); ^{13}C NMR ($CDCl_3$) δ 208.27 (e, C3), 138.39 (e, Ph), 138.33 (e, Ph), 138.21 (e, Ph), 128.24 (o, Ph), 127.77 (o, Ph), 127.65 (o, Ph), 127.52 (o, Ph), 76.65 (o), 76.45 (o), 73.80 (e), 73.25 (e), 72.48 (o, C5′), 71.34 (e), 69.81 (o, C1′), 69.08 (e), 39.57 (e, C2′), 33.43 (e, C2), 30.02 (o, C4), 25.84 (e, C1); IR (neat) cm^{-1} (μm) 3030 (3.3), 2900 (3.4), 1710 (5.8), 1495 (6.7), 1450 (7.9), 1360 (7.4), 1205 (8.3), 1090 (9.2), 910 (11.0), 740 (13.5), 695 (14.4); mass spectrum (CI), *m/z* (rel intensity) 409 (M + H, 100), 397 (14), 309 (22), 271 (15), 183 (34).

Exact mass (CI) calcd for $C_{31}H_{37}O_5$ (M + H) 489.2641, found 489.2661.

2-(3′,4′,6′-Tri-*O*-benzyl-2′-deoxy-β-D-glucopyranosyl)-1-methylpentan-4-one (β-25b). A solution of 442 mg (0.625 mmol) of stannane β-**23a** in 3.2 mL of THF at −78 °C was treated with 0.26 mL (2.49 M, 0.637 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The solution was transferred via a cooled cannula to a solution of 141 mg (0.687 mmol) of copper(I) bromide–dimethyl sulfide complex in 0.6 mL of diisopropyl sulfide and 0.7 mL of THF at −78 °C which had been treated with one drop (10 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 51 mg (60 μL, 0.521 mmol) of neat mesityl oxide (**24b**), followed by stirring at −78 °C for 2 min and addition of 98 mg (85 μL, 0.687 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 10 min, followed by warming to −50°C for 10 min, to −40 °C for 10 min, to −30 °C for 10 min to −20 °C for 10 min, and finally to 0 °C for 30 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution, followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 1 h. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 100 mL of 5% (v/v) ethyl acetate in hexane and thereafter with 8% (v/v) ethyl acetate in hexane. These procedures afforded 57 mg (20%) of δ-**25b** as a colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.33 (yellow-green spot with *p*-anisaldehyde solution); ^{1}H NMR (C_6D_6) δ 7.34–7.05 (om, 15 H, Ph), 4.99 (d, 1 H, J_{gem} = 11.3 Hz, CH_2Ph), 4.63 (d, 1 H, J_{gem} = 11.3 Hz, CH_2Ph), 4.54 (d, 1 H, J_{gem} = 11.8 Hz, CH_2Ph), 4.47 (d, 2 H, J_{gem} = 12.2 Hz, CH_2Ph), 4.41 (d, 1 H, J_{gem} = 12.3 Hz, CH_2Ph), 3.68 (m, 2 H, H6′), 3.53 (m, 2 H, $J_{2\beta'3'}$ = 11.5, $J_{2\alpha'3'}$ = 3.4 Hz, H3′, H5′), 3.36 (m, 1 H, H4′), 3.22 (dd, $J_{1'2\beta'}$ = 11.5, $J_{1'2\alpha'}$ < 2 Hz, H1′), 2.46 (d, 1 H, J_{gem} = 15.5 Hz, H3), 1.97 (d, 2 H, J_{gem} = 15.5 Hz, H3), 1.95 (ddd, 1 H, J_{gem} = 11.5, $J_{1'2\alpha'}$ < 2, $J_{2\alpha'3'}$ = 3.4 Hz, H2α′), 1.80 (s, 3 H, H5), 1.39 (ddd, 1 H, J_{gem} = 11.5, $J_{1'2\beta'}$ = 11.5, $J_{2\beta'3'}$

= 11.5 Hz, H2β'), 1.04 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 208.96 (e, C4), 138.59 (e, Ph), 128.34 (o, Ph), 128.24 (o, Ph), 127.89 (o, Ph), 127.56 (o, Ph), 127.44 (o, Ph), 81.64 (o), 80.51 (o), 78.97 (o), 78.76 (o), 74.84 (e, CH_2Ph), 73.15 (e, CH_2Ph), 71.59 (e, CH_2Ph), 69.66 (e, C6), 51.31 (e, C2), 37.14 (e, C2'), 32.32 (e, C3), 30.79 (o, C5), 24.40 (o, CH_3), 23.04 (o, CH_3); IR (neat) cm^{-1} (μm) 3030 (3.3), 2910 (3.4), 1710 (5.8), 1495 (6.7), 1450 (6.9), 1360 (7.4), 1090 (9.2), 740 (13.5), 695 (14.4); mass spectrum (CI), *m/z* (rel intensity) 517 (M + H, 100), 211 (6).

Exact mass (CI) calcd for $C_{33}H_{41}O_5$ (M + H) 517.2943, found 517.2946.

3-(3',4',6'-Tri-*O*-benzyl-2'-deoxy-β-D-glucopyranosyl)cyclohexan-1-one (β-26). A solution of 354 mg (0.500 mmol) of stannane β-**23c** in 2.5 mL of THF at −78 °C was treated with 0.21 mL (2.49 M, 0.515 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a solution of 113 mg (0.550 mmol) of copper(I) bromide–dimethyl sulfide complex in 0.6 mL of diisopropyl sulfide and 0.7 mL of THF at −78 °C which had been treated with one drop (10 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 40 mg (40 μL, 0.417 mmol) of neat cyclohex-2-en-1-one (**13**), followed by stirring at −78 °C for 3 min and addition of 78 mg (68 μL, 0.550 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 20 min, followed by warming to −50 °C for 10 min and gradual warming to −30 °C over 10 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and 200 mL of 8% (v/v) ethyl acetate in hexane and thereafter with 12% (v/v) ethyl acetate in hexane. These procedures afforded 167 mg (78%) of *C*-glycoside β-**26** as a heavy colorless oil: HPLC retention time = 10.24, 10.74 min (α-**26**, 8.63 min); TLC [20% (v/v) ethyl acetate in hexane] R_f 0.17; ^1H NMR (C_6D_6) δ 7.45–7.05 (om, 15H, Ph), 5.01 (d, 1 H, J_{gem} = 10.9 Hz, CH_2Ph), 4.65 (d, 1 H, J_{gem} = 11.0 Hz, CH_2Ph), 4.60–4.35 (od, 4 H, CH_2Ph), 3.71 (brs, 2 H, H6'), 3.52 (m, 1 H, H4'), 3.47 (om, 2 H, H3', H5'), 3.28 (m, 1 H, H1'), 2.75 (om, 2 H), 2.53 (m, 1 H), 2.25 (m, 1 H), 2.17 (om, 2 H), 1.99 (m, 2 H), 1.8 (m, 2 H), 1.7–1.1 (om); ^{13}C NMR ($CDCl_3$) δ 211.23 (e, C1), 211.14 (e, C1), 138.37 (e, Ph), 138.29 (e, Ph), 128.25 (o, Ph), 128.16 (o, Ph), 127.82 (o, Ph), 127.47 (3, Ph), 127.35 (o, Ph), 81.02 (o), 78.98 (o), 78.09 (o), 77.90 (o), 74.83 (e, CH_2Ph), 73.21 (e, CH_2Ph), 71.36 (e, CH_2Ph), 69.43 (e, C6'), 44.35 (e), 43.29 (e), 42.99 (o, C3), 41.24 (e, C2'), 41.19 (e, C2'), 33.84 (e), 33.70 (e), 27.61 (e), 26.36 (e), 24.81 (e, C4), 24.70 (e, C4); IR (neat) cm^{-1} (μm) 3030 (3.3), 2930 (3.4), 2860 (3.6), 1710 (5.8), 1495 (6.7), 1450 (6.9), 1360 (7.4), 1310 (7.6), 1260 (7.9), 1210 (8.3), 1090 (9.2), 910 (11.0), 740 (13.5), 695 (14.4); mass spectrum (CI), *m/z* (rel intensity) 515 (M + H, 100), 335 (55), 209 (62).

Exact mass (CI) calcd for $C_{33}H_{39}O_5$ (M + H) 515.2797, found 515.2800.

3-(3',4',6'-Tri-*O*-benzyl-2'-deoxy-α-D-glucopyranosyl)cyclohexan-1-one (α-26). A solution of 321 mg (0.454 mmol) of stannane α-**23c** in 2.3 mL of THF at −78 °C was treated with 0.19 mL (2.49 M, 0.463 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow-green solution was transferred via a cooled cannula to a solution of 103 mg (0.499 mmol) of copper(I) bromide–dimethyl sulfide complex in 0.5 mL of diisopropyl sulfide and 0.6 mL of THF at −78 °C which had been treated with one drop (10 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 36 mg (37 μL, 0.378 mmol) of neat cyclohex-2-en-1-one (**13**), followed by stirring at −78 °C for 3 min and addition of 71 mg (61 μL, 0.499 mmol) of boron trifluoride etherate. The solution was stirred at −78 °C for 5 min, followed by warming to −50 °C for 5 min and to 0 °C for 2 min. The solution was added to 50 mL of 1:1 NH_3–NH_4Cl solution followed by dilution with 30 mL of dichloromethane and stirring at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil. This material was chromatographed over 20 g of 200–400-mesh silica gel, eluting with 150 mL of 8% (v/v) ethyl acetate in hexane and 500 mL of 14% (v/v) ethyl acetate in hexane and thereafter with 25% (v/v) ethyl acetate in hexane. These procedures afforded 149 mg (64%) of *C*-glycoside α-**26** as a heavy colorless oil: HPLC retention time = 8.63 min (β-**26**, 10.24, 10.74 min); TLC [20% (v/v) ethyl acetate in hexane] R_f 0.08 (red-orange spot with *p*-anisaldehyde solution); ^1H NMR (C_6D_6) δ 7.40–7.05 (om, 15 H, Ph), 4.65 (m, 1 H, CH_2Ph), 4.53–4.33 (om, 5 H, CH_2Ph), 3.88 (m, 1 H), 3.72–3.46 (om, 5 H), 2.63 (m, 1 H), 2.16 (m, 2 H), 1.91–0.85 (om, 8 H); ^{13}C NMR ($CDCl_3$) δ 211.18 (e, C3), 210.82 (e, C3), 138.10 (e, Ph), 128.20 (o, Ph), 127.56 (o, Ph), 75.50 (o), 73.17 (o), 73.00 (o), 71.30 (e), 68.74 (e, C6'), 68.51 (e, C6'), 44.34 (e), 43.68 (e), 41.24 (e, C2'), 41.04 (e, C2'), 39.99 (3, C3), 39.86 (o, C3), 29.99 (e), 29.59 (e), 27.68 (e), 26.83 (e), 24.98 (e, C4), 24.62 (e, C4); IR (neat) cm^{-1} (μm) 3030 (3.3), 2920 (3.4), 2860 (3.5), 1710 (5.8), 1495 (6.7), 1450 (6.9), 1360 (7.4), 1205 (8.3), 1090 (9.2), 740 (13.5), 695 (14.4); mass spectrum (CI), *m/z* (rel intensity) 515 (M + H, 100), 407 (13), 335 (22), 317 (15), 209 (16), 181 (18).

Exact mass (CI) calcd for $C_{33}H_{39}O_5$ (M + H) 515.2797, found 515.2818.

1-(Benzyloxy)-2,2-dimethylpentan-4-one (27). A solution of 578 mg (1.405 mmol) of stannane **3** in 7.2 mL of THF at −78 °C was treated with 0.58 mL (2.49 M, 1.434 mmol) of *n*-butyllithium in hexane followed by stirring at −78 °C for 10 min. The yellow solution was transferred via a cooled cannula to a solution of 318 mg (1.546 mmol) of copper(I) bromide–dimethyl sulfide complex in 1.5 mL of diisopropyl sulfide and 1.7 mL of THF at −78 °C which had been treated with two drops (20 μL) of 2.0 M isopropylmagnesium chloride in THF as described previously, followed by stirring at −78 °C for 15 min. The brown solution was treated with 115 mg (134 μL, 1.171 mmol) of neat mesityl oxide (**24b**) followed by stirring at −78 C for 2 min and addition of 219 mg (190 μL, 1.546 mmol) of boron trifluoride etherate. The solution was allowed to warm to −50 °C over 15 min, followed by warming to 0 °C over 2 min and addition to 50 mL of 1:1 NH_3–NH_4Cl solution. The mixture was diluted with 30 mL of dichloromethane and stirred at ambient temperature for 30 min. The aqueous layer was extracted with dichloromethane (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to afford a colorless oil which was chromatographed over 12.5 g of 200–400-mesh silica gel, eluting with 100 mL of hexane and thereafter with 5% (v/v) ethyl acetate in hexane. These procedures afforded 199 mg (77%) of **27** as a colorless oil: TLC [20% (v/v) ethyl acetate in hexane] R_f 0.47 (brick-red spot with *p*-anisaldehyde solution); ^1H NMR ($CDCl_3$) δ 7.27 (s, 5 H, Ph), 4.43 (s, 2 H, CH_2Ph), 3.22 (s, 2 H, H1), 2.28 (s, 2 H, H3), 2.01 (s, 3 H, H5), 1.02 (s, 6 H, *gem*-dimethyl); IR (neat) cm^{-1} (μm) 3060 (3.3), 2960 (3.4), 2870 (3.5), 1710 (5.8), 1475 (6.8), 1355 (7.4), 1200 (8.3), 1100 (9.1), 735 (13.6), 695 (14.4); mass spectrum (EI); *m/z* (rel intensity) 162 ($M^+ - CH_3C{=}OCH_3$, 16), 91 (100), 43 (90).

Exact mass (CI) calcd for $C_{14}H_{21}O_2$ (M + H) 221.1541, found 221.1539.

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